This slide set was adapted from the 2009 Focused Update of the ACC/AHA Guidelines for Management of Patients With ST-Elevation Myocardial Infarction and the ACC/AHA/SCAI Guidelines on Percutaneous Coronary Intervention (Journal of the American College of Cardiology published ahead of print on November 18, 2009, available at:

http://content.onlinejacc.org/cgi/content/full/j.jacc.2009.10.015)

This is an update of both the STEMI and PCI 2007 focused updates & their respective 2004 & 2005 guidelines.

The full-text guidelines are also available on the Web sites:
ACC (www.acc.org) and,
AHA (www.americanheart.org)
Special Thanks to

**Slide Set Editor**

*Frederick G. Kushner, MD, FACC, FAHA, FSCAI*

and

**The 2009 STEMI Guidelines Focused Update Writing Committee Members**

Frederick G. Kushner, MD, FACC, FAHA, FSCAI, *Co-Chair*
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Michael A. Sloan, MD, MS, FACC, FAHA
Sidney C. Smith, Jr., MD, FACC, FAHA

**The 2009 PCI Guidelines Focused Update Writing Committee Members**

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David O. Williams, MD, FACC, FAHA, FSCAI‡

*2004 Writing Committee Chair
‡ SCAI Representatives
# Evolution of Guidelines for ACS

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</thead>
<tbody>
<tr>
<td>1990</td>
<td>ACC/AHA</td>
<td>AMI</td>
<td>R. Gunnar</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1994</td>
<td>AHCPR/NHLBI</td>
<td>UA</td>
<td>E. Braunwald</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>1996</td>
<td>Rev</td>
<td>Upd</td>
<td>ACC/AHA</td>
<td>AMI</td>
<td>T. Ryan</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>2004</td>
<td>Rev</td>
<td>Upd</td>
<td>ACC/AHA</td>
<td>STEMI</td>
<td>E. Antman</td>
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<td></td>
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<tr>
<td>2007</td>
<td>Upd</td>
<td>ACC/AHA</td>
<td>STEMI/PCI</td>
<td>F. Kushner</td>
<td></td>
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</tbody>
</table>
Hospitalizations in the U.S. Due to Acute Coronary Syndromes (ACS)

Acute Coronary Syndromes*

1.57 Million Hospital Admissions - ACS

UA/NSTEMI†

1.24 million Admissions per year

STEMI

.33 million Admissions per year

*Primary and secondary diagnoses. †About 0.57 million NSTEMI and 0.67 million UA.
The percentage of ACS or MI with ST elevation varies in different registries/databases.

<table>
<thead>
<tr>
<th>Registry</th>
<th>% of MI which are STEMI</th>
</tr>
</thead>
<tbody>
<tr>
<td>National Registry of Myocardial Infarction (NRMI-4)</td>
<td>29%</td>
</tr>
<tr>
<td>AHA Get with the Guidelines</td>
<td>32%</td>
</tr>
<tr>
<td>Global Registry of Acute Coronary Events (GRACE)</td>
<td>38%</td>
</tr>
</tbody>
</table>

*Primary and secondary diagnoses. †About 0.57 million NSTEMI and 0.54 million UA.
## Applying Classification of Recommendations and Level of Evidence

<table>
<thead>
<tr>
<th>Class I</th>
<th>Benefit &gt;&gt;&gt; Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedure/Treatment SHOULD be performed/administered</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Class IIa</th>
<th>Benefit &gt;&gt; Risk Additional studies with focused objectives needed</th>
</tr>
</thead>
<tbody>
<tr>
<td>IT IS REASONABLE to perform procedure/administer treatment</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Class IIb</th>
<th>Benefit ≥ Risk Additional studies with broad objectives needed; Additional registry data would be helpful</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedure/Treatment MAY BE CONSIDERED</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Class III</th>
<th>Risk ≥ Benefit No additional studies needed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedure/Treatment should NOT be performed/administered SINCE IT IS NOT HELPFUL AND MAY BE HARMFUL</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>should is recommended is indicated is useful/effective/beneficial</th>
<th>is reasonable can be useful/effective/beneficial is probably recommended or indicated</th>
<th>may/might be considered may/might be reasonable usefulness/effectiveness is unknown/unclear/uncertain or not well established</th>
<th>is not recommended is not indicated should not is not useful/effective/beneficial may be harmful</th>
</tr>
</thead>
</table>
## Applying Classification of Recommendations and Level of Evidence

<table>
<thead>
<tr>
<th>Class I</th>
<th>Class IIa</th>
<th>Class IIb</th>
<th>Class III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benefit &gt;&gt;&gt; Risk</td>
<td>Benefit &gt;&gt; Risk</td>
<td>Benefit ≥ Risk</td>
<td>Risk ≥ Benefit</td>
</tr>
<tr>
<td>Procedure/Treatment SHOULD be performed/administered</td>
<td>Additional studies with focused objectives needed</td>
<td>Additional studies with broad objectives needed; Additional registry data would be helpful</td>
<td>Procedure/Treatment MAY BE CONSIDERED</td>
</tr>
<tr>
<td>IT IS REASONABLE to perform procedure/administer treatment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Procedure/Treatment MAY BE CONSIDERED</td>
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</table>

### Level of Evidence

<table>
<thead>
<tr>
<th>Level A:</th>
<th>Level B:</th>
<th>Level C:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple populations evaluated; Data derived from multiple randomized clinical trials or meta-analyses</td>
<td>Limited populations evaluated. Data derived from a single randomized trial or non-randomized studies</td>
<td>Very limited populations evaluated. Only consensus opinion of experts, case studies, or standard-of-care.</td>
</tr>
</tbody>
</table>
Recommendations for the Use of Glycoprotein IIb/IIIa Receptor Antagonists in STEMI
It is reasonable to start treatment with glycoprotein IIb/IIIa receptor antagonists at the time of primary PCI (with or without stenting) in selected patients with STEMI:

- abciximab
- tirofiban and eptifibatide

Modified Recommendation
Use of Glycoprotein IIb/IIIa Receptor Antagonists in STEMI

<table>
<thead>
<tr>
<th>Study Name</th>
<th>Year</th>
<th>Statistics</th>
<th>p-value</th>
<th>Dead/Total</th>
<th>SM</th>
<th>GPI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valgimigli</td>
<td>2005</td>
<td>0.667 (0.11-4.09)</td>
<td>0.661</td>
<td>2/87</td>
<td>3/88</td>
<td></td>
</tr>
<tr>
<td>EVA-AMI</td>
<td>2007</td>
<td>1.017 (0.36-2.86)</td>
<td>0.974</td>
<td>8/226</td>
<td>7/201</td>
<td></td>
</tr>
<tr>
<td>MULTISTRATEGY</td>
<td>2008</td>
<td>0.438 (0.13-1.44)</td>
<td>0.173</td>
<td>4/372</td>
<td>9/372</td>
<td></td>
</tr>
<tr>
<td>FATA</td>
<td>2008</td>
<td>1.367 (0.43-4.35)</td>
<td>0.596</td>
<td>7/351</td>
<td>5/341</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.843 (0.46-1.55)</td>
<td>0.584</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The usefulness of glycoprotein IIb/IIIa receptor antagonists (as part of a preparatory pharmacologic strategy for patients with STEMI prior to arrival in the cardiac catheterization laboratory for angiography and PCI) is uncertain.
**FINESSE: Study design**

| **Treatment** | Pre-PCI treatment with $\frac{1}{2}$-dose lytic plus abciximab, pre-PCI abciximab alone, and abciximab at time of PCI |
| **Inclusion** | Suspected acute MI (ST change or LBBB) within 6 h of symptom onset |
| **Exclusion** | Low risk (<60 yo, localized inferior infarct) high risk for bleeding |
| **1° OUTCOMES** | Death, VF after 48 hours, shock, CHF within 90 days |

## Primary, secondary, and bleeding end points in FINESSE

<table>
<thead>
<tr>
<th>End point</th>
<th>Primary PCI (%)</th>
<th>Abciximab-facilitated (%)</th>
<th>Combination (abciximab/reteplase)-facilitated (%)</th>
<th>p, combination-facilitated vs primary PCI</th>
<th>p, combination-facilitated vs abciximab-facilitated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary end point* at 90 days</td>
<td>10.7</td>
<td>10.5</td>
<td>9.8</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>&gt;70% ST segment resolution within 60–90 min</td>
<td>31.0</td>
<td>33.1</td>
<td>43.9</td>
<td>0.003</td>
<td>0.01</td>
</tr>
<tr>
<td>TIMI major or minor bleeding through discharge or day 7</td>
<td>6.9</td>
<td>10.1</td>
<td>14.5</td>
<td>&lt;0.001</td>
<td>0.008</td>
</tr>
</tbody>
</table>

*All-cause mortality; rehospitalization or emergency department treatment for CHF; resuscitated ventricular fibrillation occurring >48 hours after randomization; cardiogenic shock

OnTIME 2: Study design

Acute myocardial infarction diagnosed in ambulance or referral center
ASA+600 mg Clopidogrel

Placebo

Transportation

ASA+600 mg Clopidogrel

Angiogram

Tirofiban provisional

PCI centre

Angiogram

Tirofiban cont’d

van’t Hof et al. Lancet 2008;372:537-46
**OnTIME 2: endpoints**

### Primary
- Residual ST segment deviation (>3mm) 1 hour after PCI

### Key Clinical Secondary
- Combined occurrence of death, recurrent MI, urgent TVR or thrombotic bailout at 30 days follow-up
- Safety (major bleeding)
- Death at 1 year follow-up
On-TIME 2: Results

Residual ST Deviation after PCI

van’t Hof et al. Lancet 2008;372:537-46

p=0.003  3.6 ± 4.6mm  4.8 ± 6.3mm

ACC/AHA 2009 Joint STEMI/PCI Guidelines Focused Update
**On-TIME 2: Results**

**Event-free Survival at 30 days**

<table>
<thead>
<tr>
<th>Clinical outcome</th>
<th>Placebo</th>
<th>tirofiban</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death/recurrent MI or urgent TVR</td>
<td>39/477</td>
<td>33/473</td>
<td>0.485</td>
</tr>
<tr>
<td></td>
<td>(8.2%)</td>
<td>(7.0%)</td>
<td></td>
</tr>
</tbody>
</table>

van’t Hof et al. Lancet 2008;372:537-46
## BRAVE 3: Study design

<table>
<thead>
<tr>
<th>TREATMENT:</th>
<th>pre-PCI treatment with clopidogrel (600 mg), followed by abciximab vs. placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>INCLUSION:</td>
<td>suspected acute MI (ST change or LBBB) within 24 h of symptom onset</td>
</tr>
<tr>
<td>EXCLUSION:</td>
<td>high risk for bleeding, prior trauma, thrombolytics, hypertension, relevant hematologic deviations</td>
</tr>
<tr>
<td>$1^\circ$ OUTCOMES:</td>
<td>infarct size, death, stroke, urgent revascularization of affected artery</td>
</tr>
</tbody>
</table>

Effects of Abciximab

No significant difference in infarct size or major bleeding

Mehilli et al. Circ. 2009;119:1933-1940
Recommendations for the use of Thienopyridines
Loading doses for Thienopyridines in Patients with Acute Coronary Syndromes (STEMI and UA/NSTEMI)
A loading dose of thienopyridine is recommended for STEMI patients for whom PCI is planned. Regimens should be one of the following:

Clopidogrel at least 300 mg to 600mg† should be given as early as possible before or at the time of primary or non-primary PCI.
Recommendations for the use of Thienopyridines

- The optimal loading dose of clopidogrel has not been established.

- Randomized clinical trials using >300mg of clopidogrel as a loading dose for PCI in STEMI or UA/NSTEMI have not rigorously established superior safety or efficacy.

- Clopidogrel is a prodrug which must undergo hepatic conversion to its active metabolite for platelet inhibition, a process taking several hours.
Recommendations for the use of Thienopyridines

**MODIFIED Recommendation**

Prasugrel 60 mg should be given as soon as possible for primary PCI.
TRITON-TIMI 38: Study Design

ACS (STEMI or UA/NSTEMI) & Planned PCI

ASA → N= 13,600
Double-blind

CLOPIDOGREL
300 mg LD/ 75 mg MD

PRASUGREL
60 mg LD/ 10 mg MD

1° endpoint: CV death, MI, Stroke
2° endpoints: CV death, MI, Stroke, Rehosp-Rec Isch
CV death, MI, UTVR
Stent Thrombosis (ARC definite/prob.)

Safety endpoints: TIMI major bleeds, Life-threatening bleeds

Key Substudies: Pharmacokinetic, Genomic

Median duration of therapy - 12 months

Adapted with permission from E.Antman
**TRITON: Results**

**Balance of Efficacy and Safety**

- **CV Death / MI / Stroke**
  - Clopidogrel: HR 0.81 (0.73-0.90), P=0.0004
  - Prasugrel: HR 1.32 (1.03-1.68), P=0.03
- **TIMI Major NonCABG Bleeds**
  - Clopidogrel: 12.1 events
  - Prasugrel: 138 events
- **Other Events**
  - NNT = 46
  - NNH = 167

Adapted with permission from Wiviott SD et al NEJM 357:2007

ACC/AHA 2009 Joint STEMI/PCI Guidelines Focused Update
The figure summarizes the TRITON TIMI-38 study results comparing Prasugrel and Clopidogrel in various subgroups.

**TRITON TIMI-38**

**CV Death, MI, Stroke Major Subgroups**

- **UA/NSTEMI**: Prasugrel Better with a reduction in risk of 18%.
- **STEMI**: Prasugrel Better with a reduction in risk of 21%.
- **Overall**: Prasugrel Better with a reduction in risk of 19%.

**Subgroups**

- **Age**
  - <65: Prasugrel Better with a reduction in risk of 25%.
  - 65-74: Prasugrel Better with a reduction in risk of 14%.
  - ≥75: Prasugrel Better with a reduction in risk of 6%.

- **Sex**
  - Male: Prasugrel Better with a reduction in risk of 21%.
  - Female: Prasugrel Better with a reduction in risk of 12%.

- **DM**
  - No DM: Prasugrel Better with a reduction in risk of 14%.
  - DM: Prasugrel Better with a reduction in risk of 30%.

- **CrCl**
  - CrCl > 60: Prasugrel Better with a reduction in risk of 14%.
  - CrCl < 60: Prasugrel Better with a reduction in risk of 20%.

**Wiviott SD et al. NEJM 357: 2001, 2007**
**TRITON TIMI-38**

Timing of Benefit (Landmark Analysis - 3 days)

- **Clopidogrel**
  - Loading Dose: 5.6
  - Maintenance Dose: 6.9
  - HR 0.80
  - P=0.003

- **Prasugrel**
  - Loading Dose: 4.7
  - Maintenance Dose: 5.6
  - HR 0.82
  - P=0.01

Adapted with permission from Antman EM JACC 2008.
TRITON TIMI-38

Diabetic Subgroup

N=3146

CV Death / MI / Stroke

Clopidogrel

Prasugrel

TIMI Major
NonCABG Bleeds

Clopidogrel

Prasugrel

Endpoint (%)

0 30 60 90 180 270 360 450 Days

Wiviott SD et al Circulation 2008. Adapted with permission from Antman EM.

ACC/AHA 2009 Joint STEMI/PCI Guidelines Focused Update
**TRITON TIMI-38**

**STEMI Cohort**

*N=3534*

- **CV Death / MI / Stroke**
  - **Clopidogrel**
    - 9.5%
    - HR 0.68 (0.54-0.87)
    - *P*=0.002
  - **Prasugrel**
    - 6.5%
    - HR 0.79 (0.65-0.97)
    - *P*=0.02
    - NNT = 42

- **TIMI Major NonCABG Bleeds**
  - **Clopidogrel**
    - 2.4
  - **Prasugrel**
    - 2.1

*Montalescot et al Lancet 2008. Adapted with permission from Antman EM.*

ACC/AHA 2009 Joint STEMI/PCI Guidelines Focused Update
Stent Thrombosis (ARC Definite + Probable)

Significant reductions both with BMS, DES
Significant reductions in early and late stent thromboses

HR 0.48
P < 0.0001
NNT = 77

Any Stent at Index PCI
N = 12,844

Prasugrel

Clopidogrel

Adapted with permission from Wiviott SD et al
Lancet 2008
TRITON TIMI-38: Bleeding Events Safety Cohort (N=13,457)

<table>
<thead>
<tr>
<th></th>
<th>Clopidogrel</th>
<th>Prasugrel</th>
</tr>
</thead>
<tbody>
<tr>
<td>TIMI Major Bleeds</td>
<td>1.8%</td>
<td>2.4%</td>
</tr>
<tr>
<td>ARD 0.6%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HR 1.32</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P=0.03</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NNH=167</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Life Threatening</td>
<td>0.9%</td>
<td>1.4%</td>
</tr>
<tr>
<td>ARD 0.5%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HR 1.52</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P=0.01</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonfatal</td>
<td>0.9%</td>
<td>1.1%</td>
</tr>
<tr>
<td>ARD 0.2%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P=0.23</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatal</td>
<td>0.1%</td>
<td>0.4%</td>
</tr>
<tr>
<td>ARD 0.3%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P=0.002</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ICH in Pts w Prior Stroke/TIA (N=518)</td>
<td>0.3%</td>
<td>0.3%</td>
</tr>
<tr>
<td>Clop 0 (0) %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pras 6 (2.3)%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(P=0.02)</td>
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</tbody>
</table>

ARD 0.6% HR 1.32 P=0.03 NNH=167
ARD 0.5% HR 1.52 P=0.01
ARD 0.2% P=0.23
ARD 0.3% P=0.002
ARD 0.0% P=0.74

Recommendations for the use of Thienopyridines

For STEMI patients undergoing **non-primary** PCI, the following regimens are recommended:

If the patient has received fibrinolytic therapy…

a. …and has been given clopidogrel, it should be continued as the thienopyridine of choice.

b. …without a thienopyridine, a loading dose of 300-600 mg of clopidogrel should be given as the thienopyridine of choice.

If the patient did not receive fibrinolytic therapy…

c. …either a loading dose of 300-600 mg of clopidogrel should be given or, once the coronary anatomy is known and PCI is planned, a loading dose of 60 mg of prasugrel should be given promptly and no later than 1 hour after the PCI.
The duration of Thienopyridine therapy
Thienopyridines

The duration of thienopyridine therapy should be as follows:

a. In patients receiving a stent (BMS or DES) during PCI for ACS, clopidogrel 75 mg daily† or prasugrel 10 mg § daily should be given for at least 12 months;

b. If the risk of morbidity from bleeding outweighs the anticipated benefit afforded by thienopyridine therapy, earlier discontinuation should be considered.
In patients taking a thienopyridine in whom coronary artery bypass surgery (CABG) is planned and can be delayed, it is recommended that the drug be discontinued to allow for dissipation of the antiplatelet effect.

The period of withdrawal should be at least 5 days in patients receiving clopidogrel and at least 7 days in patients receiving prasugrel, … unless the need for revascularization and/or the net benefit of the thienopyridine outweighs the potential risks of excess bleeding.
Thienopyridines

MODIFIED Recommendation

Continuation of clopidogrel or prasugrel beyond 15 months may be considered in patients undergoing drug-eluting stent placement.
Thienopyridines

NEW Recommendation

In STEMI patients with a prior history of stroke and transient ischemic attack for whom primary PCI is planned, prasugrel is not recommended as part of a dual antiplatelet therapy regimen.
Recommendations for Use of Parenteral Anticoagulants in Patients with STEMI
Use of Parenteral Anticoagulants in STEMI

Modified Recommendation

For patients proceeding to primary PCI, who have been treated with ASA and a thienopyridine, recommended supportive anticoagulant regimens include:

a. For prior treatment with UFH, additional boluses of UFH should be administered as needed to maintain therapeutic activated clotting time levels, taking into account whether GP IIb/IIIa receptor antagonists have been administered.
For patients proceeding to primary PCI, who have been treated with ASA and a thienopyridine, recommended supportive anticoagulant regimens include:

b. Bivalirudin is useful as support for primary PCI with or without prior treatment with heparin.
Bilvalirudin added as an acceptable anticoagulant for primary PCI

Unfractionated heparin (UFH) administration guided by:
- Therapeutic activated clotting time (ACT) levels
- Prior administration of GP IIb/IIIa receptor antagonists

Enoxaparin and fondaparinux unchanged from 2007 STEMI Focused Update
**HORIZONS-AMI: Design**

- **3602 patients with STEMI & symptom onset ≤ 12 hours randomized**

  - **1800 received bivalirudin alone***
    - Principal management strategy
      - Primary PCI, 1678 (93.2%)
      - Deferred PCI, 5 (0.3%)
      - CABG, 23 (1.3%)
      - Medical management, 94 (5.2%)
    - Emergency angiography

  - **1802 received heparin + GP IIb/IIIa inhibitor**
    - Principal Management Strategy
      - Primary PCI, 1662 (92.2%)
      - Deferred PCI, 3 (0.2%)
      - CABG, 40 (2.2%)
      - Medical Management, 97 (5.4%)
    - Emergency angiography

**Endpoints**: Composite of net adverse clinical events (NACE)
- Included major bleeding plus MACE (a composite of CVD death, reinfarction, target-vessel revascularization for ischemia, and stroke within 30 days)

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ACC/AHA 2009 Joint STEMI/PCI Guidelines Focused Update
**HORIZONS-AMI**: Time-to-Event Curves through 30 days: Net Adverse Clinical Events

Treatment with bivalirudin alone compared with UFH + GP IIb/IIIa Inhibitors resulted in reduced 30-day rates of net adverse clinical events

\[ \text{HR}=0.75, \ (0.62-0.92); \ p=0.006 \]

**HORIZONS-AMI**: Time-to-Event Curves through 30 days: Major Bleeding

HR = 0.59 (0.45-0.76); p<0.0001

* 40% less bleeding in Bivalirudin group at 30 days

HORIZONS-AMI: Results (cont.)

There was a statistically significant 1% increase in stent thrombosis (n=17) within the first 24 hours with bivalirudin, but no subsequent difference (1.3% versus 0.3%, p<0.001)
• Treatment with bivalirudin compared with UFH plus GP IIb/IIa inhibitors resulted in significantly lower:
  – 30-day death rates from cardiac causes (1.8% vs. 2.9%; RR 0.62; 95% CI 0.40 to 0.95; p=.03), &
  – 30-day death from all causes (2.1% vs. 3.1%; RR 0.66; 95% CI 0.44 to 1.00; p=0.047)

• At one year, MACE rates were identical, but there was a decrease in all-cause mortality with bivalirudin (3.4% versus 4.8%, p=0.03).
HORIZONS-AMI: Limitations

• Open-label design
• Administration of UFH before randomization in 66% of patients in the bivalirudin arm and 76% of patients in the UFH plus GP IIb/IIIa receptor antagonist arm
• Only 615 patients received bivalirudin monotherapy and only 60% of patients in the trial received a 600 mg clopidogrel loading dose
A preliminary report suggested that the use of bivalirudin alone (p=0.005) & a lower loading dose of clopidogrel (300 mg vs. 600 mg; p=0.01) were independent predictors of acute & subacute stent thrombosis rates, respectively.

p-values for secondary end points may not have been adjusted for multiple looks.

Recommendations for triage and transfer for Percutaneous Coronary Intervention for Patients with STEMI
NEW Recommendation

Each community should develop a STEMI system of care following the standards developed for *Mission Lifeline* including:

- Ongoing multidisciplinary team meetings with EMS, non-PCI-capable hospitals (STEMI Referral Centers), & PCI-capable hospitals (STEMI Receiving Centers)
Recommendations for Triage and Transfer for PCI (for STEMI) (cont.)

**NEW Recommendation**

STEMI system of care standards in communities should also include:

- Process for prehospital identification & activation
- Destination protocols to STEMI Receiving Centers
- Transfer protocols for patients who arrive at STEMI Referral Centers and are primary PCI candidates, and/or are fibrinolytic ineligible and/or in cardiogenic shock
It is reasonable to transfer high risk patients who receive fibrinolytic therapy as primary reperfusion therapy at a non-PCI capable facility to a PCI-capable facility as soon as possible where either PCI can be performed when needed or as a pharmacoinvasive strategy.
Recommendations for Triage and Transfer for PCI (for STEMI) (cont.)

**NEW Recommendation**

Consideration should be given to initiating a preparatory antithrombotic (anticoagulant plus antiplatelet) regimen prior to and during patient transfer to the catheterization laboratory.
Patients who are not high risk who receive fibrinolytic therapy as primary reperfusion therapy at a non-PCI capable facility may be considered for transfer to a PCI-capable facility as soon as possible where either PCI can be performed when needed or as a pharmacoinvasive strategy.
Triage and Transfer for PCI: STEMI Patients Who Are Candidates for Reperfusion

- Terms “facilitated PCI” and “rescue PCI” no longer used for the recommendations in this update
- Contemporary therapeutic choices leading to reperfusion for pts with STEMI can be described without these potentially misleading labels
Triage and Transfer for PCI: STEMI Patients Who Are Candidates for Reperfusion

• 2009 STEMI Focused Update new trials:
  – Combined Abciximab REteplase Stent Study in Acute Myocardial Infarction (CARESS-in-AMI)
  – Trial of Routine ANgioplasty and Stenting after Fibrinolysis to Enhance Reperfusion in Acute Myocardial Infarction trial (TRANSFER-AMI)
CARESS-IN-AMI: Design

- 600 STEMI pts \( \leq 75 \) years old with \( \geq 1 \) high risk feature initially treated at non-PCI hospitals with half-dose reteplase, abciximab, heparin, and ASA within 12 hours of symptom onset
- All pts randomized to immediate transfer for PCI or to standard treatment with transfer for rescue PCI if needed

**CARESS-IN-AMI:**
Study Flow Chart

600 STEMI
ASA 300-500 mg IV
Reteplase 5 U+5 U at 30 min
UFH 40 u/kg (max 3000 per u) →7 u/kg/h
Abciximab 0.25 mg/kg bolus →0.125 μg/kg/min for 12 h to a maximum 10 μg/min

299 assigned to immediate PCI
1 consent not valid
297 received reteplase
289 transferred for immediate PCI
255 received PCI

301 assigned to standard care/rescue PCI
1 consent withdrawn
298 received reteplase
107 transferred for rescue PCI
91 received PCI

**CARESS-IN-AMI: Design**

- Designed to address optimum treatment in pts for whom primary PCI not readily available
- **Not** a trial of facilitated angioplasty opposed to primary angioplasty
- Comparison between the general application of a combined pharmaco-invasive approach and the standard fibrinolysis plus selective rescue PCI approach in pts who do not qualify for primary angioplasty

Recommendations for Triage and Transfer for PCI: *High Risk Definition

- Defined in CARESS-in-AMI as STEMI patients with one or more high-risk features:
  - extensive ST-segment elevation
  - new-onset left bundle branch block
  - previous MI
  - Killip class >2, or
  - left ventricular ejection fraction ≤35% for inferior MIs;
- Anterior MI alone with 2 mm or more ST-elevation in 2 or more leads qualifies

CARESS-IN-AMI: Study Results

- PCI was performed in 85.6% of patients in the immediate PCI group & rescue PCI was performed in 30.3% of the standard treatment/transfer for rescue PCI group.
- There was a shorter median fibrinolytic therapy-to-PCI center transfer time in the immediate vs. rescue PCI groups (110 min vs 180 min, p<0.0001).

**CARESS-IN-AMI:** Primary Outcome

primary outcome (composite of all cause mortality, reinfarction, & refractory MI within 30 days) occurred significantly less often in the immediate PCI group vs. standard care/rescue PCI group.

CARESS-IN-AMI: Study Results

- No significant differences in the rates of major bleeding at 30 days (3.4% versus 2.3%, p=0.47) or stroke (0.7% versus 1.3%, p=0.50) between groups

**CARESS-IN-AMI: Implications**

- High-risk STEMI patients treated at non-PCI hospitals with a preparatory pharmacologic strategy of half-dose fibrinolytic therapy, abciximab, heparin, & ASA have improved outcomes when transferred immediately to a PCI facility rather than continuing medical therapy with transfer for rescue PCI only if there is evidence of failed reperfusion.
TRANSFER-AMI

Study of pharmacoinvasive strategy in 1059 patients with STEMI presenting to non-PCI-capable hospitals within 12 hrs of symptom onset & with ≥ 1 high-risk feature

Recommendations for Triage and Transfer for PCI: *High Risk Definition*

- Defined in TRANSFER-AMI as $\geq 2$ mm ST-segment elevation in 2 anterior leads or ST elevation at least 1 mm in inferior leads with at least one of the following:
  - systolic blood pressure $<100$ mm Hg
  - heart rate $>100$ beats per minute
  - Killip Class II-III
  - $\geq 2$ mm of ST-segment depression in the anterior leads
  - $\geq 1$ mm of ST elevation in right-sided lead V4 indicative of right ventricular involvement

TRANSFER-AMI--Design

• All patients were treated with fibrinolytic therapy and randomized to:
  – a pharmaco-invasive strategy (immediate transfer for PCI within 6 hours of fibrinolytic therapy) or to
  – standard treatment after fibrinolytic therapy (included rescue PCI as required for ongoing chest pain and less than 50% resolution of ST-elevation at 60-90 minutes or hemodynamic instability).

TRANSFER-AMI--Design (cont.)

• Standard treatment patients who did not require rescue PCI remained at the initial hospital for at least 24 hours and coronary angiography within the first 2 weeks encouraged.

• All patients received standard-dose tenecteplase (TNK), ASA, and either UFH or enoxaparin.

TRANSFER-AMI--Design (cont.)

- Clopidogrel loading (300 mg for patients < 75 years of age, and 75 mg ≥ 75 years of age) strongly encouraged in all study patients
- GP IIb/IIIa receptor antagonists administered at the PCI-capable hospitals according to institutions’ standard practice

# TRANSFER-AMI: Results Procedures

<table>
<thead>
<tr>
<th></th>
<th>Pharmaco-invasive vs. Standard Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median time to TNK</td>
<td>Approximately 2 hrs in both groups</td>
</tr>
<tr>
<td>administration from</td>
<td></td>
</tr>
<tr>
<td>symptom onset</td>
<td></td>
</tr>
<tr>
<td>Median time from</td>
<td>2.8 hrs vs. 32.5 hrs</td>
</tr>
<tr>
<td>TNK to catheterization</td>
<td></td>
</tr>
<tr>
<td>Coronary angiography</td>
<td>98.5% vs. 88.7%</td>
</tr>
<tr>
<td>PCI performed</td>
<td>84.9% vs. 67.4%</td>
</tr>
</tbody>
</table>

TRANSFER-AMI--Safety Results

- Incidence of TIMI major and minor bleeding and GUSTO moderate and severe bleeding was not different between groups.
- There was higher incidence of GUSTO mild bleeding in the pharmaco-invasive group (13.0% compared to 9.0% in the standard treatment group, p=0.036).

TRANSFER-AMI Study Conclusion

• Following treatment with fibrinolytic therapy in high risk STEMI pts presenting to hospitals without PCI-capability, transfer to a PCI center to undergo coronary angiography and PCI should be initiated immediately without waiting to determine whether reperfusion has occurred.

Pathway: Triage and Transfer for PCI (in STEMI)

STEMI patient who is a candidate for reperfusion

Initially seen at a PCI capable facility
- Send to Cath Lab for primary PCI (Class I, LOE:A)
  - Prep antithrombotic (anticoagulant plus antiplatelet) regimen
  - Diagnostic angio
    - Medical therapy only
    - PCI
    - CABG

Initially seen at a non-PCI capable facility
- Transfer for primary PCI (Class I, LOE:A)
  - At PCI facility, evaluate for timing of diagnostic angio

HIGH RISK
- Transfer to a PCI facility is reasonable for early diagnostic angio & possible PCI or CABG (Class IIa, LOE:B), High-risk patients as defined by 2007 STEMI Focused Update should undergo cath (Class 1: LOE B)

NOT HIGH RISK
- Transfer to a PCI facility may be considered (Class IIb, LOE:C), especially if ischemic symptoms persist and failure to reperfuse is suspected

Initial Treatment with fibrinolytic therapy (Class 1, LOE:A)
Pathway: Triage and Transfer for PCI (in STEMI)

- Those presenting to a **non-PCI-capable facility** should be triaged to **fibrinolytic therapy or** immediate transfer for PCI.
- Decision depends on multiple clinical observations that allow judgment of:
  - mortality risk of the STEMI
  - risk of fibrinolytic therapy
  - duration of the symptoms when first seen
  - time required for transport to a PCI-capable facility
Pathway: Triage and Transfer for PCI (in STEMI)  

- If primary PCI is chosen, the patient will be transferred for PCI.
- If fibrinolytic therapy is chosen, the patient will receive the agent(s) and a judgment as to whether the patient is high risk or not will be determined.
Pathway: Triage and Transfer for PCI (in STEMI)—(cont.)

• If high risk, the patient should receive appropriate antithrombotic therapy and be moved immediately to a PCI-capable facility for diagnostic catheterization and consideration of PCI.
• If not high risk, the patient may be moved to a PCI-capable facility after receiving antithrombotic therapy, or observed in the initial facility
Pathway: Triage and Transfer for PCI (in STEMI)—(cont.)

• Patients best suited for transfer for PCI are STEMI pts:
  – Presenting with high-risk features
  – High bleeding risk from fibrinolytic therapy
  – Late presenters-->4 hrs after onset of symptoms

• Decision to transfer is a judgment made considering the time required for transport and the capabilities of the receiving hospital
Pathway: Triage and Transfer for PCI (in STEMI) — (cont.)

• STEMI pts best suited for fibrinolytic therapy are those presenting early after symptom onset with low bleeding risk

• After fibrinolytic therapy, if not high risk, transfer to a PCI-capable facility may be considered, especially if symptoms persist and failure to reperfuse is suspected.
Triage and Transfer for PCI (in STEMI)

- The duration of symptoms should continue to serve as a modulating factor in selecting a reperfusion strategy for STEMI patients.
- While patients at high risk (e.g., CHF, shock, contraindications to fibrinolytic therapy) are best served with timely PCI, inordinate delays between the time from symptom onset and effective reperfusion with PCI may prove deleterious, especially among the majority of STEMI patients at relatively low risk.
Each community and each facility in that community should have an agreed-upon plan for how STEMI patients are to be treated, including:

- which hospitals should receive STEMI patients from EMS units capable of obtaining diagnostic ECGs
- management at the initial receiving hospital, and
- written criteria & agreements for expeditious transfer of patients from non-PCI-capable to PCI-capable facilities
Triage and Transfer for PCI (in STEMI)

• Need for the development of regional systems of STEMI care through stakeholder efforts to evaluate ACS care using:
  – standardized performance & quality improvement measures, (e.g., endorsed by the ACC, AHA, Joint Commission, Centers for Medicare and Medicaid Services)
  – standardized quality-of-care data registries designed to track and measure outcomes, complications and adherence to evidence-based processes of care
    • NCDR ACTION Registry ®
    • American Heart Association “Get With the Guidelines”
Triage and Transfer for PCI (in STEMI)

- American Heart Association’s *Mission Lifeline* is an initiative to encourage closer cooperation and trust amongst prehospital care providers, and cardiac care professionals.
Recommendations for Intensive Glucose Control in STEMI
Intensive Glucose Control in STEMI

NEW Recommendation

It is reasonable to use an insulin based regimen to achieve and maintain glucose levels less than 180 mg/dl while avoiding hypoglycemia for patients with STEMI with either a complicated or uncomplicated course.
Recommendations for Thrombus Aspiration during PCI for STEMI
Thrombus Aspiration During PCI for STEMI

NEW Recommendation

Aspiration thrombectomy is reasonable for patients undergoing primary PCI
Recommendations for the use of stents in STEMI
Use of stents in STEMI

NEW Recommendation

It is reasonable to use a drug-eluting stent as an alternative to a bare-metal stent for primary PCI in STEMI.

*Consideration for the use of stents (DES or BMS) in STEMI should include the ability of the patient to comply with prolonged dual antiplatelet therapy, the bleeding risk in patients on chronic oral anticoagulation, and the possibility that the patient may need surgery during the ensuing year.
Use of stents in STEMI

MODIFIED Recommendation

A DES may be considered for clinical and anatomic settings† in which the efficacy/safety profile appears favorable.
PCI focused update section
Recommendations for angiography in patients with chronic kidney disease
In patients with chronic kidney disease undergoing angiography and who are not on chronic dialysis, either an isosmolar contrast medium or a low molecular weight contrast medium other than ioxaglate or iohexol is indicated.
The indications for contrast agents during angiography or PCI in patients with chronic kidney disease are now expanded to include both iso osmolar and low molecular weight agents other than ioxaglate or iohexol.
Relative renal safety of iodixanol vs. IOCM: Meta-analysis, Reed et al

Variations in relative renal safety by specific LOCM

• Reduction in CIN observed when iodixanol vs. ioxaglate & iohexol
• No difference in comparisons of iodixanol with iomeprol, iopamidol, iopromide, or ioversol
Nephrotoxicity of iodixanol vs. LOCM: Meta Analysis

Heinrich et al.

Trends in CIN favoring iodixanol no longer significant


ACC/AHA 2009 Joint STEMI/PCI Guidelines Focused Update
RR of CIN for comparison of iodixanol with iohexol and nonionic LDCM other than iohexol

RR (95% CI) Weight (%) Study RR (95% CI) Weight (%)

Sinha 2004 (ab) 0.22 (0.05-0.96) 13.1 Heinrich MC et al. Radiology. 2009;250:68-86.
Aspelin 2003 0.44 (0.22-0.88) 56.7 Kuhn 2006 0.87 (0.30-2.52) 8.4
Chalmers 1999 0.36 (0.07-1.75) 11.0 Thomsen 2008 1.32 (0.37-4.72) 5.9
Siegel 1996 1.17 (0.32-4.32) 16.2 Hardiek 2008 1.32 (0.26-1.51) 12.1
Hill 1994 0.20 (0.01-4.03) 3.0 Solomon 2007 1.26 (0.73-2.19) 31.3
Schmid 2007 0.97 (0.06-19.06) 1.3 Feldkamp 2006 1.24 (0.50-3.10) 11.3
Barrett 2006 1.01 (0.21-4.86) 3.9 Rudnick 2005 (ab) 1.00 (0.33-1.32) 19.5
Kolehmainen 2003 (ab) 1.00 (0.22-4.49) 4.2 Carraro 1998 3.00 (0.13-71.03) 0.9
Fischbeck 1996 0.95 (0.08-14.13) 1.3

Overall 0.45 (0.26-0.76)

Test for Heterogeneity
Q = 3.3, df = 4, p = 0.51, I^2 = 0
Test for Overall Effect
Z = -3.00, p < 0.01

Overall 0.97 (0.72-1.32)

Test for Heterogeneity
Q = 4.1, df = 10, p = 0.94, I^2 = 0
Test for Overall Effect
Z = -0.17, p = 0.86

p=NS, indicates equivalent safety
Recommendations for the use of Fractional Flow Reserve
Use of FFR

Coronary pressure (fractional flow reserve [FFR]) or Doppler velocimetry can be useful to determine whether PCI of a specific coronary lesion is warranted. FFR or Doppler velocimetry can also be useful as an alternative to performing noninvasive functional testing (e.g., when the functional study is absent or ambiguous) to determine whether an intervention is warranted.

It is reasonable to use intracoronary physiologic measurements (coronary pressure [FFR]) (Level of Evidence: A)

or Doppler velocimetry (Level of Evidence: C)) in the assessment of the effects of intermediate coronary stenoses (30% to 70% luminal narrowing) in patients with anginal symptoms.
**Use of FFR**

**Routine** assessment with intracoronary physiologic measurements such as coronary pressure (FFR) or Doppler ultrasound to assess the severity of angiographic disease in concordant vascular distribution in patients with angina and a positive, unequivocal noninvasive functional study is not recommended.
FAME

Assessed for Eligibility
N=1905

Randomized
N=1005

Angiography-guided PCI
N=496
Lost to follow-up
N=11
Analyzed
N=496

FFR-guided PCI
N=509
Lost to follow-up
N=8
Analyzed
N=509

Not eligible N= 900
Left main stenosis  N= 157
Extreme coronary tortuosity or calcification  N= 217
No informed consent  N= 105
Contra-indication for DES  N= 86
Participation in other study  N= 94
Logistic reasons  N= 210
Other reasons N= 31

Tonino et al. N Engl J Med. 2009;360;213-224. Adapted with permission from Fearon W.
FAME: Results

**Trial design:** Patients with multivessel disease were randomized to either routine angiography-guided PCI or fractional flow reserve (FFR)-guided PCI, with stenting of only those lesions with an FFR of ≤0.8. Clinical outcomes were compared at 1 year.

**Results**
- Resource utilization (contrast: 272 vs. 302 ml, cost of procedure ($5,332 vs. $6,007) shorter with FFR-guided PCI compared with routine PCI (all p < 0.05)
- MACE lower at 1 year with FFR (p = 0.02)
- Incidence of death (p = 0.19), MI (p = 0.07), and CABG or re-PCI (p = 0.08) at 1 year were similar

**Conclusions**
- FFR-guided PCI is associated with a lower incidence of MACE compared with angiography-guided PCI in patients with multivessel disease, with a decrease in resource utilization
- Further studies validating these findings are necessary

Recommendations for PCI for Unprotected Left Main Coronary Artery Disease
PCI of the left main coronary artery using stents as an alternative to CABG may be considered in patients with anatomic conditions that are associated with low risk of PCI procedural complications and Clinical conditions that predict an increased risk of adverse surgical outcomes.*
PCI for unprotected left main

It is reasonable that patients undergoing PCI to unprotected left main coronary obstructions be followed up with coronary angiography between 2 and 6 months after PCI.
## Outcomes of PCI vs. CABG for Unprotected Left Main

<table>
<thead>
<tr>
<th>Author/Year (Reference)</th>
<th>Type of Study (recruitment years)</th>
<th>PCI/CABG</th>
<th>Short-term Results</th>
<th>Long-term Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chieffo 2006</td>
<td>Cohort 2002-2004</td>
<td>107/142</td>
<td>In-hospital outcomes for PCI versus CABG: Death: 0% versus 2.1%, <em>P</em>=NS MI: 9.3% versus 26.1%, <em>P</em>=0.0009 Stroke: 0% versus 2%, <em>P</em>=NS</td>
<td>1-Year adjusted ORs for PCI versus CABG: Death or MI: 0.26;95% CI 0.078–0.597; <em>P</em>=0.0005 Death, MI, or stroke: 0.385; 95% CI 0.180–0.819; <em>P</em>=0.01 Revascularization: 4.2; 95% CI 1.486–14.549; <em>P</em>=0.005</td>
</tr>
<tr>
<td>Lee 2006</td>
<td>Cohort 2003-2005</td>
<td>50/123</td>
<td>30-Day outcomes for PCI versus CABG: Death: 2% versus 5%; <em>P</em>=NS MI: 0% versus 2%; <em>P</em>=NS Stroke: 0% versus 8%; <em>P</em>=0.03 Death/MI/stroke/revascularization: 17% versus 2%; <em>P</em>&lt;0.01</td>
<td>1-Year follow-up for PCI versus CABG: Death: 4% versus 15%; <em>P</em>=0.2 Death, MI, stroke: 4% versus 21%; HR=4.4; 95% CI 1.0–18.6; <em>P</em>=0.03 Revascularization: 13.3% versus 5.5%; <em>P</em>=0.2</td>
</tr>
<tr>
<td>Author/Year (Reference)</td>
<td>Type of Study (yrs of recruitment)</td>
<td>PCI/CABG</td>
<td>Short-term Results</td>
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</tr>
</tbody>
</table>
| Palmerini 2006          | Cohort 2002-2005                  | 157/154  | 30-Day outcomes for PCI versus CABG:  
Death: 3.2% versus 4.5%; \( P=NS \)  
MI: 4.5% versus 1.9%; \( P=NS \)  
Revascularization: 0.6% versus 0.6%; \( P=NS \) | 1- to 2-Year follow-up for PCI and CABG:  
Death: 13.4% versus 12.3%; 95% CI 0.51–1.77; \( P=0.8 \)  
MI: 8.3% versus 4.5%; 95% CI 0.21-1.32; \( P=0.17 \)  
Revascularization: 2.6% versus 25.5%; 95% CI 0.03–0.23; \( P=0.0001 \) |
| Buszeman 2008           | Randomized 2001-2004              | 52/53    | 30-Day outcomes for PCI versus CABG:  
Death: 0% versus 0%  
MI: 2% versus 4%; \( P=NS \)  
MACE: 2% versus 14%; 95% CI 0.79-0.99; \( P=0.03 \) | 1-Year follow-up for PCI versus CABG:  
Death: 2% versus 8%; \( P=NS \)  
MI: 2% versus 6%; \( P=NS \)  
Revascularization: 30% versus 10%; 95% CI 1.05–1.54; \( P=0.01 \)  
MACE: 32% versus 26%; 95% CI 0.85–1.38; \( P=NS \) |
<table>
<thead>
<tr>
<th>Author/Year (Reference)</th>
<th>Type of Study (yrs of recruitment)</th>
<th>PCI/CABG</th>
<th>Short-term Results</th>
<th>Long-term Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sanmartin 2007</td>
<td>Cohort 2000-2005</td>
<td>96/245</td>
<td>30-Day outcomes for PCI versus CABG: Death: 2.1% versus 6.1%; (P=0.17) Death/MI/stroke/revascularization: 2.1% versus 9.0%; (P=0.03)</td>
<td>1 year for PCI vs. CABG: Death: 5.2% versus 8.4%; (P=0.37) MI: 0% versus 1.3%; (P=0.44) Repeat revascularization: 5.2% versus 0.8%; (P=0.02) Death/MI/stroke/revascularization: 10.4% versus 11.4%; (P=0.5)</td>
</tr>
<tr>
<td>Brener 2008</td>
<td>Cohort with matched CABG controls 1997-2006</td>
<td>97/190</td>
<td></td>
<td>At 3 years, outcomes for PCI versus CABG: Death: 20% versus 15%; (P=0.14)</td>
</tr>
<tr>
<td>Author/Year (Reference)</td>
<td>Type of Study (yrs of recruitment)</td>
<td>PCI/CABG</td>
<td>Short-term Results</td>
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<tr>
<td>Seung 2008</td>
<td>Matched Cohort 2000-2006</td>
<td>542/542</td>
<td></td>
<td>At 3 years, HRs for PCI versus CABG: Death: 1.18; HR=1.18; 95% CI 0.77–1.80; P=0.45 Death/MI/stroke: 1.10; HR=1.10;, 95% CI 0.75–1.62; P=0.61, Revascularization: 4.76; HR=4.76; 95% CI 2.80–8.11; P&lt;0.001</td>
</tr>
<tr>
<td>White 2008</td>
<td>Cohort 2003-2007</td>
<td>120/223</td>
<td></td>
<td>At 30 months, HRs for PCI vs. CABG; Death 1.93; 95% CI 0.89-4.19; p=0.10</td>
</tr>
<tr>
<td>Serruys 2009</td>
<td>Randomized 2005-2007</td>
<td>348/357</td>
<td></td>
<td>At 1 year, HRs for PCI versus CABG: Death/MI/CVA/revascularization: 15.8 versus 13.7;, P=0.44</td>
</tr>
</tbody>
</table>
Recommendations for the timing of Angiography and Antiplatelet Therapy in UA/NSTEMI
Patients with definite or likely UA/NSTEMI selected for an invasive approach should receive dual-antiplatelet therapy. Aspirin should be initiated on presentation. Clopidogrel (before or at the time of PCI) (*Level of Evidence: A*)

*or*

prasugrel (at the time of PCI) (*Level of Evidence: B*) is recommended as a second antiplatelet agent.
Recommendations for the Timing of Angiography and Antiplatelet Therapy in UA/NSTEMI

NEW Recommendation

It is reasonable for initially stabilized high-risk patients with UA/NSTEMI* (GRACE [Global Registry of Acute Coronary Events] risk score > 140) to undergo an early invasive strategy within 12 to 24 hours of admission. For patients not at high risk, an early invasive approach is also reasonable.
**TIMACS: Study design**

<table>
<thead>
<tr>
<th><strong>Treatment</strong></th>
<th>Routine early intervention (coronary angiography within 24 hours) or delayed (coronary angiography at 36 hours+)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Inclusion</strong></td>
<td>NSTE-ACS (no ST elevation within 24 hours of symptom onset) &amp; high risk</td>
</tr>
<tr>
<td><strong>Exclusion</strong></td>
<td>Not suitable for revascularization</td>
</tr>
<tr>
<td><strong>1° OUTCOMES</strong></td>
<td>Death, MI, stroke at 6 mo.</td>
</tr>
<tr>
<td><strong>2° OUTCOMES</strong></td>
<td>Refractory ischemia</td>
</tr>
</tbody>
</table>

TIMACS: Results

No significant difference in rate of death, new MI or stroke at 6 mo.

HR = 0.85 (95% CI, 0.68-1.06)

P = 0.15

Early intervention significantly improved outcomes in highest risk patients

TIMACS: Results

Secondary Outcome:
Early-intervention group had a 28% reduction in death, MI, or refractory ischemia compared to the delayed-intervention group.

HR, 0.72 (0.58-0.89)
P=0.003

Dosing Table for Antiplatelet and Anticoagulant Therapy Discussed in This Focused Update to Support PCI in STEMI

<table>
<thead>
<tr>
<th>Drug</th>
<th>During PCI</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Patient received initial medical treatment (with an anticoag &amp;/or lytic therapy)</td>
<td>▶ All patients to receive ASA (162–325 mg)</td>
</tr>
<tr>
<td>Glycoprotein IIb/IIa receptor antagonists</td>
<td>Patient did not receive initial medical treatment (with an anticoag &amp;/or lytic therapy)</td>
<td></td>
</tr>
<tr>
<td>Abciximab</td>
<td>Of uncertain benefit</td>
<td>▶ Continue for up to 12 hrs at the discretion of the physician</td>
</tr>
<tr>
<td></td>
<td>LD of 0.25 mg/kg IV bolus MD of 0.125 mcg/kg per minute (maximum 10 mcg/min) (Class IIa, LOE:A)</td>
<td></td>
</tr>
<tr>
<td>Eptifibatide</td>
<td>Of uncertain benefit</td>
<td>▶ Double bolus recommended to support PCI in STEMI as the recommended adult dosage of eptifibatide in patients with normal renal function. ▶ Infusion should be continued for 12-18 hrs at the discretion of the physician.</td>
</tr>
<tr>
<td></td>
<td>LD of 180 mcg/kg IV bolus followed 10 minutes later by second IV bolus of 180 mcg/kg MD of 2.0 mcg/kg per minute, started after first bolus; reduce infusion by 50% in patients with estimated creatinine clearance &lt; 50 mL/min (Class IIa, LOE:B)</td>
<td></td>
</tr>
<tr>
<td>Tirofiban</td>
<td>Of uncertain benefit</td>
<td>▶ Increased dosing over previous recommendation. ▶ Continue for up to 18 hrs at the discretion of the physician.</td>
</tr>
<tr>
<td></td>
<td>LD of 25 mcg/kg IV bolus MD of IV infusion of 0.1 mcg/kg/min; reduce rate of infusion by 50% in patients with estimated creatinine clearance &lt; 30 mL/min (Class IIa, LOE:B)</td>
<td></td>
</tr>
</tbody>
</table>
### Dosing Table for Antiplatelet and Anticoagulant Therapy Discussedin This Focused Update to Support PCI in STEMI

<table>
<thead>
<tr>
<th>Drug</th>
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</tr>
</thead>
<tbody>
<tr>
<td><strong>Thienopyridines</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clopidogrel†</td>
<td>Patient received initial medical treatment (with an anticoag &amp;/or fibrinolytic therapy)</td>
<td>✷ All patients to receive ASA (162–325 mg)</td>
</tr>
<tr>
<td></td>
<td>If 600 mg given orally, then no additional treatment</td>
<td></td>
</tr>
<tr>
<td></td>
<td>A second LD of 300 mg may be given orally to supplement a prior LD of 300 mg (Class I, LOE:C)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Patient did not receive initial medical treatment (with an anticoag &amp;/or fibrinolytic therapy)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>LD 300–600 mg orally</td>
<td></td>
</tr>
<tr>
<td></td>
<td>MD of 75 mg orally per day (Class I, LOE: C)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>✷ optimal LD has not been established</td>
<td></td>
</tr>
<tr>
<td></td>
<td>✷ Dose for patients &gt;75 years old has not been established.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>✷ A recommended duration of therapy exists for all post-PCI patients</td>
<td></td>
</tr>
<tr>
<td></td>
<td>receiving a BMS or DES.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>✷ Period of withdrawal before surgery should be at least 5 days.</td>
<td></td>
</tr>
<tr>
<td>Prasugrel</td>
<td>No data available</td>
<td>✷ There is no clear need for treatment with prasugrel before PCI.</td>
</tr>
<tr>
<td>Drug</td>
<td>During PCI</td>
<td>Comments</td>
</tr>
<tr>
<td>----------------------</td>
<td>---------------------------------------------------------------------------</td>
<td>--------------------------------------------------------------------------</td>
</tr>
<tr>
<td></td>
<td>Patient received initial medical treatment (with an anticoag &amp;/or lytic therapy)</td>
<td>All patients to receive ASA (162–325 mg)</td>
</tr>
<tr>
<td></td>
<td>Patient did not receive initial medical treatment (with an anticoag &amp;/or lytic therapy)</td>
<td></td>
</tr>
<tr>
<td>Prasugrel ‡(cont.)</td>
<td>MD of 10 mg orally per day (Class I, LOE: B)</td>
<td>MD of 5 mg orally per day in special circumstances.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Special dosing for patients &lt;60 kg or &gt;75 years of age.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>There is a recommended duration of therapy for all post-PCI patients receiving a DES.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Contraindicated for use in patients with prior history of TIA or stroke.</td>
</tr>
<tr>
<td>Drug</td>
<td>During PCI</td>
<td>Comments</td>
</tr>
<tr>
<td>------------</td>
<td>---------------------------------------------------------------------------</td>
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<td></td>
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<td></td>
</tr>
<tr>
<td></td>
<td>Patient did not receive initial medical treatment (with an anticoag &amp;/or lytic therapy)</td>
<td></td>
</tr>
<tr>
<td>Bivalirudin</td>
<td>For patients who have received UFH, wait 30 minutes, then give 0.75 mg/kg bolus, then 1.75 mg/kg per hour infusion (<em>Class I, LOE: B</em>)</td>
<td>0.75 mg/kg bolus, 1.75 mg/kg per hour infusion. <em>Bivalirudin may be used to support PCI &amp; STEMI with or without previously administered UFH with the addition of 600 mg of clopidogrel.</em> <em>In STEMI patients undergoing PCI who are at high risk of bleeding, bivalirudin anticoagulation is reasonable.</em></td>
</tr>
<tr>
<td>UFH</td>
<td>IV GP IIb/IIIa planned: target ACT 200–250 seconds. No IV GP IIb/IIIa planned: target ACT 250–300 seconds for HemoTec, 300–350 seconds for Hemochron (<em>Class I, LOE: C</em>)</td>
<td>IV GP IIb/IIIa planned: 50–70 U/kg bolus to achieve an ACT of 200–250 seconds. No IV GP IIb/IIIa planned: 70–100 U/kg bolus to achieve target ACT of 250–300 seconds for HemoTec, 300–350 seconds for Hemochron (<em>Class I, LOE: C</em>)</td>
</tr>
</tbody>
</table>
Thank You